

XX Claim 4; Fig 1; 88pp; English.

CC This is the amino acid sequence of Tango-63d, a new member of the
 CC human tumour necrosis factor receptor superfamily. It was deduced
 CC from a human prostate cDNA clone sequence (see V62672). 2
 CC Different forms of Tango-63, i.e. Tango-63d and Tango-63e (see
 CC W79261), have been identified. These are identical with the
 CC exception of the deletion of amino acids 183-211 of Tango-63d in
 CC Tango-63e. The invention also encompasses nucleic acid molecules
 CC encoding Tango-63d and -63e, vectors containing these nucleic acid
 CC molecules, cells harboring recombinant DNA encoding Tango-63d and/or
 CC -63e, fusion proteins that include Tango-63d and/or -63e, transgenic
 CC animals that express Tango-63d and/or -63e, and recombinant knockout
 CC animals that fail to express Tango-63d and/or -63e. Methods are
 CC provided for the diagnosis and treatment of disorders associated
 CC with either an abnormally high or an abnormally low rate of
 CC apoptotic cell death. Inhibitors can be used for treating e.g.
 CC cancers, autoimmune disorders (e.g. systemic lupus erythematosus
 CC and immune-mediated glomerulonephritis), and viral infections (e.g.
 CC herpesviruses, poxviruses, and adenoviruses). Agonists can be used
 CC for treating e.g. neurodegenerative diseases, e.g. Alzheimer's
 CC disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS),
 CC Huntington's disease, retinitis pigmentosa, spinal muscular atrophy,
 CC various forms of cerebellar degeneration, anaemia, myelodysplastic
 CC syndrome, ischemic injury, myocardial infarction, cerebral ischemia
 CC or toxin-induced injury. In addition, T cell mediated diseases,
 CC including AIDS, autoimmune diseases such as rheumatoid arthritis,
 CC and type I diabetes, septic shock, cerebral malaria, graft
 CC rejection, cytotoxicity, cachexia, and inflammation can be treated
 CC by altering the expression or activity of the polypeptides. The
 CC products can also be used for detection, diagnosis and screening
 CC assays.

XX Sequence 440 AA:

Query Match 99.6%; Score 2317; DB 19; Length 440;

Best Local Similarity 99.8%; Pred. No. 3 6e-185; Indels 0; Gaps 0;

Matches 439; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MDRGONAPASGARRKHPGPREARGARBPVPTLVVAALLVSAESALITQOD 60
 DB 1 megrgnapaasgarckrhpgpreargarpqlrvpklvlvvaavlllvsaesalltqgd 60
 QY 61 LAPQRAAQQRRSSSEGLCPGGHHISDGRICISCKTGGQDSTWMDLRLCTRCD 120
 DB 61 lapqraaqqkrrsspsglcpghhisdgricisckkygqdstwmdllrlctrcd 120
 QY 121 SGEVELSPCTTRNTVQCQCEGTFREDESPEMCRKCRTPGMVAVGCTPMSDIECVH 180
 DB 121 sgevelspcttrntvqcqceegtfredepemcrkcrtpgmvavgdctpsdiecvh 180
 QY 181 KESGTHSGEADPAVEFTVSSPCTPASPCSLGIIIGTVAAVLVAVFVCKSLIMKXY 240
 DB 181 kesgthsgadpaaveftvsspctpaspslsglligtvaavllvavfvckslimkxy 240
 QY 241 LVYKIGTCGGGGDPRVRSORPGEADNVINEIVSIIOPOVROEVOEPAPPTGV 300
 DB 241 lvykigtcggggdprvrsorpgeadnvineivsiilqpqvpeqnevgpaeptgv 300
 QY 301 NMLSPSESHLEPAEARSORRRLLVPANEGDPTFLRQCEPDFADLVFPDSWEPLMRK 360
 DB 301 nmlspseeshlepaearssrrllvpanegdptflrqcepdfadlvfpdswemlrmk 360
 QY 361 LGIMDNEIVAKAEAGHDTLYTMLIKVNTKGRDASVHTLLDALETGERAKRKIED 420
 DB 361 lgimdneivakaeaghdlytmlikvntkgrdasvhtlldaletgerlarkkied 420
 QY 421 HLISGKFWYLEGNDASMS 440
 DB 421 hlisgkfwylegndasms 440

RESULT 2

ID Y05725 standard; Protein: 440 AA.

AC Y05725;

DT 19-JUL-1999 (first entry)

DE Tumour necrosis factor receptor TRAIL-R2.

KW TRAIL-2; tumour necrosis factor receptor; apoptosis; cancer;

KW therapy.

OS Mammalia.

FT Key

FT Peptide

FT Protein

FT Region

FT Region

FT Domain

FT Domain

FT Domain

FT Domain

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Query Match 99.4%; Score 2313; DB 20; Length 440;

Best Local Similarity 99.5%; Pred. No. 7.7e-185;

PS Disclosure: Page 27; 28pp; English.

The present sequence represents TRAIL-R2, a novel mammalian
 CC cysteine-rich receptor of the tumour necrosis factor receptor family.
 CC The invention is related to novel receptors for TRAIL, i.e. TRAIL-2
 CC and TRAIL-3 (see Y05726). TRAIL-2 is structurally similar to the
 CC death domain-containing receptor TRAIL-R1. Its cytoplasmic domain
 CC binds to the adaptor molecules FADD and TRADD, and can also
 CC associate with TRAIL-R1, suggesting that TRAIL may signal through a
 CC TRAIL-R1/TRAIL-R2 heteroreceptor signalling complex. TRAIL-R2
 CC shows a broad tissue distribution. A method for preventing or
 CC reducing the advancement, severity or effects of an immunological
 CC disease involves administering a TRAIL-R2 or TRAIL-R3 blocking
 CC agent such as a soluble TRAIL-R (preferably comprising a human
 CC immunoglobulin Fc domain) and an antibody. A method of treating
 CC cancer involves administration of antibodies against TRAIL-R3 or
 CC TRAIL-R2. A method of inducing cell death involves administration
 CC of an agent capable of inhibiting the binding of TRAIL-R2 or -R3 to
 CC its ligand.

Sequence 440 AA:

Matches 438; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 1 MEORGNAPASGARRKHGPREANGARPGPRVPTLVVVAALLVSAESALITOOD 60
 Db 1 megrgnapaasgartrhpgpreargarpglrvpklvlvaavallvsaesalltqgd 60

QY 61 LAPQORAAPOQRSSPSEGLCPRGHHISDGRDCISCKYGODYSTHMDLLECLRCTRCD 120
 Db 61 lapqorvabqqrsspsglcprghhlsedgrdcisckygodysthmndllecrlctcd 120

QY 121 SGVEELSPCTTTRNTVCOCEEGTFREDESPEMCRKRTGCPRGMAVVGDCPTMSDIECVH 180
 Db 121 sgveelsptcttrntvcoceegtfreedspemcrkrtgcprgmvvgdcptmsdiecvh 180

QY 181 KESGTHSGEPAPVETVSSPCTPASPCSLGIITGVVAAVLVAVFVCKSLIMKKV 240
 Db 181 kesgthsgpapvetvsspctpaspslsgliigtvvaavllvavfvckslimkkv 240

QY 241 LPYLKIGCSGGGDPERVDSSQRPAGEDNVLEIVSIIQPTQVPOEMEVOEPAPPTGV 300
 Db 241 lpylkgicsgggdpervdssqrpaednvleivsiilqptqvpoemevogepapptgv 300

QY 301 NMLSPSESHLEPAAERSQRRRLVLPANEGDPTETLRQCFDPAFLVPFDSWEPLMK 360
 Db 301 nmlspseeshlepaaersqrrllvpanegdptetlrqctfdpafldvpfdsweplmk 360

QY 361 LGIMDEIKVAKAEAGHRDLYTMLIKVWNTGRDASVHTLLDALETGERLAKKIED 420
 Db 361 lgimdelkvakeaaghndlytmlikvwnktgrdasvhtlldaletgerlakkiied 420

QY 421 HLISGKFWLEGNDASAMS 440
 Db 421 hlissgkfmylegndasams 440

RESULT 3
 B01340 B01340 standard; Protein: 440 AA.

AC B01340;
 DT 25-SEP-2000 (first entry)
 DE TNF-related apoptosis inducing ligand (TRAIL) receptor-2.
 KW UL144; death receptor; apoptosis; programmed cell death; FAS;
 KW TNF-R1; TRAMP; DR-6; TRAIL; modulation; treatment; cancer; virus;
 KW human.
 OS Homo sapiens.
 PN WO200034335-A2.
 PD 15-JUN-2000.
 PF 03-DEC-1999; 99WO-US26035.
 PR 04-DEC-1998; 98US-0205018.
 PA (SCHE) SCHERING CORP.
 PI Leong C, Phillips JH;
 DR WPI; 2000-423383/36.
 PT Purified or recombinant polypeptide for modulating apoptosis comprises
 PT a sequence which binds to an antibody specific for UL144 or its
 PT fragments
 PS Disclosure: Page 71-73; 76pp; English.
 CC A pure or recombinant polypeptide which binds to a polyclonal antibody
 CC specific for the mature UL144 is useful for screening molecules which

CC block induction of apoptosis or interfere with antiapoptotic activity.
 CC The polypeptide is also useful for modulating apoptosis and useful in
 CC treatment of conditions associated with abnormal physiology or
 CC development, such as cancer or degenerative conditions and for
 CC regulation of viral infection and replication. At least five
 CC different death receptors are known, which include the CD95
 CC (Fas/Apo-1), the TNF receptor-1, TNF receptor apoptosis-mediated
 CC protein (TRAMP), death receptor-6 (DR-6), and TNF-related
 CC apoptosis-inducing ligand (TRAIL) receptors 1, 2 and 4.

SQ Sequence 440 AA:

Query Match 99.4%; Score 2313; DB 21; Length 440;
 Best local similarity 99.5%; Pred. No. 7.7e-185;
 Matches 438; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 1 MEORGNAPASGARRKHGPREANGARPGPRVPTLVVVAALLVSAESALITOOD 60
 Db 1 megrgnapaasgartrhpgpreargarpglrvpklvlvaavallvsaesalltqgd 60

QY 61 LAPQORAAPOQRSSPSEGLCPRGHHISDGRDCISCKYGODYSTHMDLLECLRCTRCD 120
 Db 61 lapqorvabqqrsspsglcprghhlsedgrdcisckygodysthmndllecrlctcd 120

QY 121 SGVEELSPCTTTRNTVCOCEEGTFREDESPEMCRKRTGCPRGMAVVGDCPTMSDIECVH 180
 Db 121 sgveelsptcttrntvcoceegtfreedspemcrkrtgcprgmvvgdcptmsdiecvh 180

QY 181 KESGTHSGEPAPVETVSSPCTPASPCSLGIITGVVAAVLVAVFVCKSLIMKKV 240
 Db 181 kesgthsgpapvetvsspctpaspslsgliigtvvaavllvavfvckslimkkv 240

QY 241 LPYLKIGCSGGGDPERVDSSQRPAGEDNVLEIVSIIQPTQVPOEMEVOEPAPPTGV 300
 Db 241 lpylkgicsgggdpervdssqrpaednvleivsiilqptqvpoemevogepapptgv 300

QY 301 NMLSPSESHLEPAAERSQRRRLVLPANEGDPTETLRQCFDPAFLVPFDSWEPLMK 360
 Db 301 nmlspseeshlepaaersqrrllvpanegdptetlrqctfdpafldvpfdsweplmk 360

QY 361 LGIMDEIKVAKAEAGHRDLYTMLIKVWNTGRDASVHTLLDALETGERLAKKIED 420
 Db 361 lgimdelkvakeaaghndlytmlikvwnktgrdasvhtlldaletgerlakkiied 420

QY 421 HLISGKFWLEGNDASAMS 440
 Db 421 hlissgkfmylegndasams 440

RESULT 4
 W79083 W79083 standard; Protein: 411 AA.

AC W79083;
 DT 11-JAN-1999 (first entry)
 DE Human death domain containing receptor 5 (DR5).
 KW Death domain containing receptor 5; DR5; human; apoptosis;
 KW tumour necrosis factor receptor; cancer; autoimmune disease;
 KW inflammation; infection; AIDS; graft versus host disease;
 KW neurodegeneration; systemic lupus erythematosus;
 KW glomerulonephritis; rheumatoid arthritis; graft rejection;
 KW osteoarthritis; psoriasis; septicemia; inflammatory bowel disease;
 KW Alzheimer's disease; Parkinson's disease; retinitis pigmentosa;
 KW amyotrophic lateral sclerosis; aplastic anaemia; leukaemia;
 KW septic shock; cachexia; anorexia; agonist; antagonist; therapy;
 KW diagnosis.
 OS Homo sapiens.
 XX

FH Key Location/Qualifiers
 FT Peptide 1..51
 FT /label= Sig_peptide
 FT Protein 52..411
 FT /label= Mat_protein
 FT Domain 52..184
 FT /label= Extracellular
 FT Domain 185..208
 FT /label= Transmembrane
 FT Domain 209..411
 FT /label= Intracellular
 FT Domain 324..391
 FT /label= Death
 FN WO9841629-A2.
 XX 24-SEP-1998.
 XX 17-MAR-1998; 98WO-US05377.
 XX 29-JUL-1997; 97US-0054021.
 PR 17-MAR-1997; 97US-0040846.
 XX (HUMA-) HUMAN GENOME SCI INC.
 PA Gentz RL, Ni J, Rosen CA, Su JY, Yu G;
 PI WPI: 1998-531568/45.
 DR N-PSDB; V61469.
 XX New isolated death domain containing receptor 5 - used to develop
 PT products for treating e.g. cancers, autoimmune disorders, viral
 PT infections, inflammation, graft-versus-host disease or
 PT neurodegenerative disorders
 PT
 PT
 PS Claim 4; Fig 1A-B; 89pp; English.
 XX
 CC This is the amino acid sequence of human death domain containing
 CC receptor 5 (DR5), deduced from an isolated DR5 nucleic acid (see
 CC V61469). DR5 is a novel member of the tumour necrosis factor
 CC receptor (TNFR) family that has been shown to bind TRAIL, and which
 CC has the ability to induce apoptosis. It shows homology to human
 CC TNFR1, FAS and DR3. DR5 cDNA has been identified in primary
 CC dendritic cells, endothelial tissue, spleen, chronic lymphocytic
 CC leukaemia, and human thymus stromal cells. The isolated nucleic
 CC acid can be used in the recombinant production of DR5 polypeptides,
 CC e.g. the extracellular, transmembrane, intracellular domains,
 CC mature protein or soluble polypeptides lacking the transmembrane
 CC domain, vectors, host cells and recombinant methods of producing
 CC the polypeptides are claimed. DR5 polypeptides can be used to
 CC identify agonists and antagonists, and to raise antibodies.
 CC Agonists, which increase DR5 mediated signalling, can be used to
 CC treat diseases in which decreased apoptosis is exhibited, e.g.
 CC cancers, autoimmune disorders (such as systemic lupus erythematosus
 CC and immune-related glomerulonephritis rheumatoid arthritis) and
 CC viral infections (such as herpes viruses, pox viruses and
 CC adenoviruses), inflammation, graft versus host disease, acute graft
 CC rejection, chronic graft rejection, rheumatoid arthritis,
 CC osteoarthritis, psoriasis, septicemia, and inflammatory bowel
 CC disease. Antagonists, which decrease DR5 mediated signalling, can
 CC be used to treat diseases in which apoptosis is exhibited, e.g.
 CC AIDS, neurodegenerative disorders (such as Alzheimer's disease,
 CC Parkinson's disease, amyotrophic lateral sclerosis, retinitis
 CC pigmentosa, cerebellar degeneration), myelodysplastic syndromes
 CC (such as aplastic anaemia), ischemic injury (such as that caused by
 CC myocardial infarction, stroke and reperfusion injury), toxin-induced
 CC liver disease (such as that caused by alcohol), septic shock,
 CC cachexia and anorexia. The products can also be used for detection,
 CC diagnosis and drug screening.
 XX Sequence 411 AA:

Query Match 92.5%; Score 2151.5; DB 19; Length 411;
 Best Local Similarity 93.4%; Pred. No. 2,1e-171;
 Matches 411; Conservative 0; Mismatches 0; Indels 29; Gaps 1;
 QY 1 MEORGNAPASGARKRRHGPGEARGARBPVPTLVVAVALLVSAESALITQOD 60
 DB 1 megrgnapaasgarkrbgppreargarpprvkltlvvaavllvsaesalltqgd 60
 QY 61 LAPQORARPOQRSSPSELCPPGHHISDGDICSKRGDYSYRHMNDLFLCARTCD 120
 DB 61 lapqoraarpqorsspselcpgghhisdgdicskrgdystrhmndlflcrtcd 120
 QY 61 lapqraapqqrsspselcpgghhisdgdicskrgdystrhmndlflcrtcd 120
 DB 61 lapqraapqqrsspselcpgghhisdgdicskrgdystrhmndlflcrtcd 120
 QY 121 SCEVELSPCTTRNTVCCCECTPREDESPKCRKCRTPGKAVGDCPTWSDIECVH 180
 DB 121 sgevelspcttrntvcccectpredeSPKCRKCRTPGKAVGDCPTWSDIECVH 180
 QY 181 KESGTHSGEADPAVEETVTSPTPASCSLSGIIIGVTAAVLLIVAEVCKSLMKKV 240
 DB 181 ke-----sglllgvtvaavllivaevfckslmkkv 211
 QY 241 LPYLKIGICSGGSDPERVDRSSQRCAPENVAETIVSLIQPVQEOEMEVEPAPPTGV 300
 DB 212 lpylkigicsggdpervdrssqrcapenvaetivslilqpvqegemevepapeptgv 271
 QY 301 NMISPGSESHLEPAEERSQRRLLVPANEGDPTETLRQCFDPAFLVPFDSWEPLMRK 360
 DB 272 nmispgeseshllepaeeersqrrllvpaneqdpetlrrqcfddfadlvpfswepmrk 331
 QY 361 LGLMNEIKVANAEEAGHRDLYTMLIKWNKTGSDASVHTLLDLLETLGELAKQIED 420
 DB 332 lglmneikvanaeeaghrdlytmlikwnktgdsavhtlldlletlgerlakqied 391
 QY 421 HLLSGKEMYLEGNADSAMS 440
 DB 392 hllssgkemylegnadsams 411
 RESULT 5
 ID W93608 standard; Protein; 411 AA.
 AC W93608;
 XX 18-JUN-1999 (first entry)
 DE Human killer adriamycin-inducible protein.
 KW Killer protein; adriamycin inducible; human; chromosome 8p21; diagnosis;
 KW p53-inducible; apoptosis-mediating activity; treatment; animal model;
 KW neoplastic disease.
 OS Homo sapiens.
 PN W09902653-A1.
 PD 21-JAN-1999.
 PF 10-JUL-1998; 98WO-US14495.
 XX 11-MAR-1998; 98US-0077661.
 PR 11-JUL-1997; 97US-0052305.
 PR 04-AUG-1997; 97US-0054710.
 PR 30-SEP-1997; 97US-0060473.
 PR 11-MAR-1998; 98US-0077526.
 PR 11-MAR-1998; 98US-0077628.
 PA (UYPE-) UNIV PENNSYLVANIA.
 PI El-Deliry WS;
 XX WPI: 1999-120857/10.
 DR N-PSDB; X23721.
 XX

PT A new nucleic acid encodes a p53-induced protein (killer) - which induces apoptosis and is useful in the diagnosis and treatment of neoplastic diseases

PS Claim 8; Page 44; 65pp; English.

CC This invention describes a novel human adriamycin-inducible killer protein located on chromosome 8p21, which also has p53-inducible, apoptosis-mediated activity and comprises an amino-terminal extracellular receptor, transmembrane and death domains. The nucleic acid molecule which encodes the protein, its encoded signal transduction protein and antibodies of the invention are useful in the diagnosis and treatment of neoplastic diseases. The invention is also useful for the production of animal model systems.

CC

XX Sequence 411 AA:

SO

Query Match 92.5%; Score 2151.5; DB 20; Length 411;
Best Local Similarity 93.4%; Pred. No. 2.1e-171;
Matches 411; Conservative 0; Mismatches 0; Indels 29; Gaps 1;

QY 1 MEORGWAPASGARKHGPGPREARGARPGPRVPTLVVAVALLVSAESALITQOD 60
DB 1 meqrgnapaasgaarkhpgpreargarpgprvptklvvaavallvsaesalltqgd 60

QY 61 LABQARAAPQOKRSSPSEGLCPGHHISEDRGRCISCKYQDYSTHWNDLFLCRLTRCD 120
DB 61 lapqraapqokrsspsseglcpghhisedrgrcisckygdysthwndlflcltrctcd 120

QY 121 SGEVELSPTTTNTNTVQCCEGTFREDSPEMKRCKTGCRGMVKYGDCTPMSDIECVH 180
DB 121 sgevelsptcttntntvccegtfreedspemcrkctgcrgmvkvgdctpmsdiecvh 180

QY 121 sgevelsptcttntntvccegtfreedspemcrkctgcrgmvkvgdctpmsdiecvh 180

QY 181 KESGTHSGAPAVEEVTSSPGTPASPCSLGIIIGVTAAVVLVAVVCKSLMKKV 240
DB 181 ke-----sglllgvtvaavvlvavvckslmkkv 211

QY 241 LPYLKIGICSGGGDPERVRRSSORPGAEDNVLEIVSILOPTOVPEQEMVQPAEPTGV 300
DB 212 lpylkigicsgggdpervrrssorpgaednvleivsiiloptovpeqemvqpaeptgv 271

QY 301 NMLSPGSEHLLEPAEAKRSQRRRLVPAVEGPTETLRQCFDPADLVDPDSWEPIARK 360
DB 272 nmlspgsehllepaeakrsqrrrlvpanegptetlrcqcfddpdlvpdswepimrk 331

QY 361 LGLMDNEIKYAKAEAGHRTLTMLIKWNKGRDASVHTLLDALETLGERLAKOKIED 420
DB 332 lglmdneikyakaeaghrtdltymlikwnkgrdasvhtlldaletlgerlakokied 391

QY 421 HLSSGKFMYLEGNADSAMS 440
DB 392 hlssgkfmylegnadsams 411

RESULT 6
B29790
ID B29790 standard; Protein: 411 AA.
XX B29790;
AC B29790;
DT 28-FEB-2001 (first entry)
XX
DE Human death domain containing receptor-5 (DR5).
XX
KW Human death domain containing receptor-5; DR5; anti-DR5 antibody;
KW TRAIL binding; TNF-related apoptosis-inducing ligand; pro-apoptotic;
KW tumour necrosis factor related apoptosis family; TNFR; graft-versus-host disease;
KW viral infection; cancer; leukaemia; immunodeficiency; autoimmune disease;
KW T-cell mediated immune response; osteoarthritis; psoriasis; septicemia;
KW inflammatory bowel disease; parasitic infection; bacterial infection;
KW restenosis.
XX

OS Homo sapiens.
XX
PN WO200006156-A1.
XX
PD 09-NOV-2000.
XX
PF 04-MAY-2000; 2000MO-US12041.
XX
PR 04-MAY-1999; 9905-0132498.
XX
PR 07-MAY-1999; 9905-0133238.
XX
PR 13-AUG-1999; 9905-0148939.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI NI J, Gentz RL, Yu G, Rosen CA;
XX
PI WPI; 2000-687447/67.
XX
DR N-PSDB; C81544.
XX
PT Treating graft-versus-host disease, viral infection, cancer, leukemia,
PT immunodeficiency, or an autoimmune disorder comprising administering an
PT antibody to death domain containing receptor (DR5) and a second agent -
XX
PS Claim 1; Fig 1A-B; 266pp; English.

CC The invention relates to a novel method for treating graft-versus-host disease, viral infection, cancer, leukemia, immunodeficiency, or an autoimmune disorder. The method comprises administering an antibody specific for human death domain containing receptor-5 (DR5; B29790) and a second agent selected from TRAIL (TNF-related apoptosis-inducing ligand), a tumor necrosis factor (TNF), a TNF blocking agent, an immunosuppressive agent, an antibody, an anti-inflammatory agent, a chemotherapeutic agent, or a cytokine. DR5 is a member of the TNF receptor (TNFR) family, and is a mediator of apoptosis, being able to bind TRAIL. The method of the invention is useful for the treatment of CC graft-versus-host disease, viral infection, cancer, leukemia, CC immunodeficiency, or an autoimmune disorder. The DR-5 antibody is useful CC for treating or preventing diseases and conditions associated with CC increased cell survival and/or insensitivity to apoptosis-inducing CC agents. Examples of such diseases are solid tissue cancers and CC leukemias. Antagonists of DR5 are useful for inhibiting T-cell mediated CC immune responses, and preventing and/or treating diseases and conditions CC associated with T-cell mediated immune responses such as graft-versus- CC host responses, osteoarthritis, psoriasis, septicemia, inflammatory CC bowel disease, autoimmune diseases and leukemia. DR5 nucleotides and CC proteins are useful for diagnosis, prevention and/or treatment of CC parasitic, bacterial, and viral infections, restenosis and autoimmune CC disorders. The present sequence represents human DR5.

CC

XX Sequence 411 AA:

SO

Query Match 92.5%; Score 2151.5; DB 21; Length 411;
Best Local Similarity 93.4%; Pred. No. 2.1e-171;
Matches 411; Conservative 0; Mismatches 0; Indels 29; Gaps 1;

QY 1 MEORGWAPASGARKHGPGPREARGARPGPRVPTLVVAVALLVSAESALITQOD 60
DB 1 meqrgnapaasgaarkhpgpreargarpgprvptklvvaavallvsaesalltqgd 60

QY 61 LABQARAAPQOKRSSPSEGLCPGHHISEDRGRCISCKYQDYSTHWNDLFLCRLTRCD 120
DB 61 lapqraapqokrsspsseglcpghhisedrgrcisckygdysthwndlflcltrctcd 120

QY 121 SGEVELSPTTTNTNTVQCCEGTFREDSPEMKRCKTGCRGMVKYGDCTPMSDIECVH 180
DB 121 sgevelsptcttntntvccegtfreedspemcrkctgcrgmvkvgdctpmsdiecvh 180

QY 121 sgevelsptcttntntvccegtfreedspemcrkctgcrgmvkvgdctpmsdiecvh 180

QY 181 KESGTHSGAPAVEEVTSSPGTPASPCSLGIIIGVTAAVVLVAVVCKSLMKKV 240
DB 181 ke-----sglllgvtvaavvlvavvckslmkkv 211

QY 241 LPYLKIGICSGGGDPERVRRSSORPGAEDNVLEIVSILOPTOVPEQEMVQPAEPTGV 300

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Db 212 |pylkgicgsgggdperdrssqrpaednvnleivslilqprqypegemeveqepetgv 271
Qy 301 |NMLSPGESEHLLPEPAEERSQRRLLVPANEGDPTETLRQCDFDPADLVPEPDSWEPLMRK 360
Db 272 |nmlspgeeshllpepaersqrrllvpanegdptetlrqctdfadlvpfdsweplmrk 331
Qy 361 |IGLMDNEIKVAKAEAGHRDILYMLIKWNTGSDASVHTLLDLPLETGERLAKOKIED 420
Db 332 |lgldneikvakaaghrdilymlikwntgrdasvhtlldaletigerlakqkied 391
Qy 421 |HLSSGKFMYLEGNADSAMS 440
Db 392 |hlssgkfmylegnadsams 411

RESULT 7
ID W76827 standard; Protein: 411 AA.
XX W76827;
AC W76827;
DT 25-JAN-1999 (first entry)
DE Human TR6 protein.
XX
KW TR6; tumour necrosis factor related receptor; human; treatment; stroke;
KW inflammation; arthritis; septicemia; autoimmune disease; restenosis;
KW transplant rejection; infection; ischaemia; brain injury; bone disease;
KW acute respiratory disease syndrome; acquired autoimmune disease syndrome;
KW AIDS; cancer; atherosclerosis; Alzheimers disease.
XX
OS Homo sapiens.
XX
PN EP870827-A2.
XX
PD 14-OCT-1998.
XX
PE 23-DEC-1997; 97EP-0310562.
XX
PR 22-AUG-1997; 97US-0916625.
PR 14-MAR-1997; 97US-0041230.
PR 09-MAY-1997; 97US-0853684.
XX
PA (SMIK ) SMITHKLINE BEECHAM CORP.
XX
PI Deen KC, Young PR;
XX
DR WPI: 1998-523156/45.
DR N-PSDB: V63094.
XX
PT DNA encoding tumour necrosis factor receptor TR6 - and corresponding
PT polypeptide, antibody, agonist, antagonist, etc
XX
PS Claim 1; Page 27-29; 34pp; English.
XX
CC This sequence represents a novel human tumour necrosis factor related
CC receptor, TR6. TR6 polypeptides and polynucleotides can be used in the
CC treatment of chronic and acute inflammation, arthritis, septicemia,
CC autoimmune diseases (e.g. inflammatory bowel disease, psoriasis),
CC transplant rejection, graft vs. host disease, infection, stroke,
CC ischaemia, acute respiratory disease syndrome, restenosis, brain injury,
CC (acquired autoimmune disease syndrome) AIDS, bone diseases, cancer (e.g.
CC lympho-proliferative disorders), atherosclerosis and Alzheimers disease.
XX
SQ Sequence 411 AA;

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Query Match 92.1%; Score 2143.5; DB 19; Length 411;
Best Local Similarity 93.2%; Pred. No. 9,8e-171;
Matches 410; Conservative 0; Mismatches 1; Indels 29; Gaps 1;
Qy 1 MEORGONAPPAAGARRKRGPGPREARGARPGPRVPTLVLVAAVLLIVSASALITQOD 60

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Db 1 |meqrgqnappaasgarkrlgpppreargarpgrvptklivlvaavallivsaesalltqgd 60
Qy 61 |LAPQORAPAOQRKSSPSBGLCPGHHISFDGDCISCKYGDGYSTHWMDLFLCLACTGCD 120
Db 61 |lapqorapaoqrksspsbglcpgghisfdgdcisckygdystcwmndllfclactgcd 120
Qy 121 |SGEVELSPCTTTRNMTVCCOEEGTFRDEDEPEWCRKCRFGCPGMYKVGDCPWSDECVH 180
Db 121 |sgevelspctttrnmtvcceegtfrdeedepemcricrctgprgmkygdcpswdecvh 180
Qy 181 |KESGTRKHSGEAPAVEETVTSPTPASPCSLGIIIGVTAAVLLIVAVFYCKSLMKRV 240
Db 181 |kesgtrkhsgeapaveetvtsptpaspcslgiiigtvaavllivavfycslmkrv 211
Qy 241 |PYLKGICGSGGGDPERDRSSQRRGAEENVLEIVSLILOPQVPEOMEVQEPAPETGV 300
Db 212 |pylkgicgsgggdperdrssqrpaednvnleivslilqprqypegemeveqepetgv 271
Qy 301 |NMLSPGESEHLLPEPAEERSQRRLLVPANEGDPTETLRQCDFDPADLVPEPDSWEPLMRK 360
Db 272 |nmlspgeeshllpepaersqrrllvpanegdptetlrqctdfadlvpfdsweplmrk 331
Qy 361 |IGLMDNEIKVAKAEAGHRDILYMLIKWNTGSDASVHTLLDLPLETGERLAKOKIED 420
Db 332 |lgldneikvakaaghrdilymlikwntgrdasvhtlldaletigerlakqkied 391
Qy 421 |HLSSGKFMYLEGNADSAMS 440
Db 392 |hlssgkfmylegnadsams 411

RESULT 8
ID W79261 standard; Protein: 411 AA.
XX W79261;
AC W79261;
DT 15-FEB-1999 (first entry)
DE
XX
KW Tumour necrosis factor receptor related protein Tango-63e.
KW Tango-63e; tumour necrosis factor receptor related protein; human;
KW apoptosis; cancer; autoimmune disease; neurodegenerative disease.
XX
OS Homo sapiens.
XX
PN WO9846643-A1.
XX
PD 22-OCT-1998.
XX
PE 16-APR-1998; 98WO-US07694.
XX
PR 16-APR-1997; 97US-0843652.
XX
PA (MILL-) MILLENNIUM BIOTHERAPEUTICS INC.
XX
PI Holtzman D;
XX
DR WPI: 1998-594562/50.
DR N-PSDB: V62673.
XX
PT Isolated tumour necrosis factor related proteins - used to develop
PT products for the diagnosis and treatment of apoptosis-related
PT disorders, e.g. cancers, autoimmune disorders or neurodegenerative
PT disorders
XX
PS Claim 6; Fig 2; 88pp; English.
XX
CC This is the amino acid sequence of Tango-63e, a new member of the
CC human tumour necrosis factor receptor superfamily. It was deduced
CC from a human prostate cDNA clone sequence (see V62673). Two
CC different forms of Tango-63, i.e. Tango-63e and Tango-63d (see

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CC W79260), have been identified. These are identical with the
 CC exception of the deletion of amino acids 183-211 of Tango-63d in
 CC Tango-63e. The invention also encompasses nucleic acid molecules
 CC encoding Tango-63d and -63e, vectors containing these nucleic acid
 CC molecules, cells harboring recombinant DNA encoding Tango-63d and/or
 CC -63e, fusion proteins that include Tango-63d and/or -63e, transgenic
 CC animals that express Tango-63d and/or -63e, and recombinant knockout
 CC animals that fail to express Tango-63d and/or -63e. Methods are
 CC provided for the diagnosis and treatment of disorders associated
 CC with either an abnormally high or an abnormally low rate of
 CC apoptotic cell death. Inhibitors can be used for treating e.g.
 CC cancers, autoimmune disorders (e.g. systemic lupus erythematosus
 CC and immune-mediated glomerulonephritis), and viral infections (e.g.
 CC herpesviruses, poxviruses, and adenoviruses). Agonists can be used
 CC for treating e.g. neurodegenerative diseases, e.g. Alzheimer's
 CC disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS),
 CC Huntington's disease, retinitis pigmentosa, spinal muscular atrophy,
 CC various forms of cerebellar degeneration, anaemia, myelodysplastic
 CC syndrome, ischemic injury, myocardial infarction, cerebral ischemia
 CC or toxin-induced injury. In addition, T cell mediated diseases,
 CC including AIDS, autoimmune diseases such as rheumatoid arthritis,
 CC and type I diabetes, septic shock, cerebral malaria, graft
 CC rejection, cytotoxicity, cachexia, and inflammation can be treated
 CC by altering the expression or activity of the polypeptides. The
 CC products can also be used for detection, diagnosis and screening
 CC assays.

XX Sequence 411 AA:

Query Match 92.0%; Score 2141.5; DB 19; Length 411;
 Best Local Similarity 93.2%; Pred. No. 1.4e-170;

Matches 410; Conservative 0; Mismatches 1; Indels 29; Gaps 1;

QY 1 MEORGNAPASGARRRHPGPREARGARPRVPTLVVAVALLVASASALLTQOD 60
 DB 1 megrgnapaasgartrhpgpreargarprglrvpklvlvaavallvsaeasalltqgd 60
 QY 61 LAPQQAAPQOKRSSPSEGLCPGHHIISDGRDCISCKYGDVSTHWNLLFCLRCTRCD 120
 DB 61 lapqqaapqokrsspseglcpghhisedgrdciscskygdydsthwnllfclrtctcd 120
 QY 121 SGEVELSPCTTTRNTVCOCEEGTFREEDSPEMCRKCRGCPGMYKVGDCPTWSDIECVH 180
 DB 121 sgevelspctttrntvcoceegtfreedspemcrkcrtgcpmykvvgdcptwsdiecvh 180
 QY 181 KESGTHSEBAVAERTVSSPCTPASPCSLGIIIGVVAVALLVAVFVCKSLMKKV 240
 DB 181 ke-----sglllgvvaavllvavfvckslmkkv 211
 QY 241 LPLKIGCGGGGDPPEVRSSORPGADNVLNEIYSIIOPVPOEMEVOPAPPTGV 300
 DB 241 lplkigcgggdppevrssorpgadnvlneiysiiopvpoemevopapptgv 300
 QY 301 NMLSPGESEHLEPAPAEERSQRRRLVPANEGDPTETLRQCFDDFADLVFPDSMEPLMRK 360
 DB 301 nmlspgesehlepapaeersqrrrlvpanegdptetlrqcfddfdlvfpdsmeplmrk 360
 QY 361 LGLMNEIVAAAEAGHDTLYTLIKVNTKGRDASVHTLLDALETGERLAKKIED 420
 DB 361 lglmneivaaaeaghdtlytlmkvntkgrdasvhtlldaletgerlakkie 420
 QY 421 HLSSGKFWYLEGNDASAMS 440
 DB 421 hlssgkfwylegnadsams 411

RESULT 9
 ID W93576
 XX W93576 standard; Protein: 411 AA.
 AC W93576;
 XX

DT 18-JUN-1999 (first entry)
 XX
 DE Human hAPO8 protein.
 XX
 KW Tumour necrosis factor receptor; signal transducer molecule; TNF; APO4;
 KW developmental abnormality; gestational abnormality; prostate cancer;
 KW APO6; APO8; APO9; TNFR-1; TNFR-3; diagnosis; treatment; therapy; disease;
 KW cytoplasmic domain; immunogen; antibody preparation; breast carcinoma;
 KW apoptosis; human.
 XX
 OS Homo sapiens.
 XX
 PN W09911791-A2.
 XX
 PD 11-MAR-1999.
 XX
 PE 04-SEP-1998; 98WO-US18393.
 XX
 PR 05-SEP-1997; 97US-0924634.
 XX
 PA (UNITED STATES) WASHINGTON.
 XX
 PI Chaudhary PM;
 XX
 DR WPI: 1999-205191/17.
 XX
 DR N-PSDB: X23410.
 XX

PT New Tumour Necrosis Factor family receptor polypeptides and ligands -
 PT useful for diagnosis and treatment of prostate cancer and
 PT developmental or gestational abnormalities
 PS Claim 19; Fig 2; 156pp; English.

CC This invention describes isolated Tumour Necrosis Factor (TNF) family
 CC receptor polypeptides: APO4, APO6, APO8 and APO9 or their active
 CC fragments, and isolated TNF related ligands 1 and 3 (TNRL1 and TNRL3) or
 CC their active fragments. APO4 is useful for diagnosing prostate cancer
 CC by determining levels of APO4 in an individual. Prostate cancer can also
 CC be treated using APO4 selective binding agents linked to a therapeutic
 CC moiety. APO4 polypeptides are also useful for identifying selective
 CC binding agents, useful in diagnosis/treatment of disease by binding of
 CC agents to the polypeptide/active fragment which is extracellular, or
 CC expressed on the cell surface. The binding is preferably performed in
 CC vivo. APO4 polypeptides/active fragments are also useful for screening
 CC for agonists and antagonists by binding and observing the change in APO4
 CC activity. Effective pharmacological agents useful in diagnosis or
 CC treatment of disease are also identified using APO4 polypeptides/active
 CC fragments and APO4 signal transducer molecules that specifically interact
 CC with a cytoplasmic domain of APO4 and detecting a change in level of APO4
 CC activity. The method is performed in vivo or in vitro. APO polypeptides
 CC are all useful as immunogens for preparing antibodies. APO4 is also
 CC useful for diagnosis/treatment of developmental or gestational
 CC abnormalities. APO8 was transfected to human breast carcinoma cell line
 CC MCF-7, and induced apoptosis.

XX Sequence 411 AA:

Query Match 91.9%; Score 2137.5; DB 20; Length 411;
 Best Local Similarity 93.0%; Pred. No. 3.1e-170;
 Matches 409; Conservative 0; Mismatches 2; Indels 29; Gaps 1;

QY 1 MEORGNAPASGARRRHPGPREARGARPRVPTLVVAVALLVASASALLTQOD 60
 DB 1 megrgnapaasgartrhpgpreargarprglrvpklvlvaavallvsaeasalltqgd 60
 QY 61 LAPQQAAPQOKRSSPSEGLCPGHHIISDGRDCISCKYGDVSTHWNLLFCLRCTRCD 120
 DB 61 lapqqaapqokrsspseglcpghhisedgrdciscskygdydsthwnllfclrtctcd 120
 QY 121 SGEVELSPCTTTRNTVCOCEEGTFREEDSPEMCRKCRGCPGMYKVGDCPTWSDIECVH 180
 DB 121 sgevelspctttrntvcoceegtfreedspemcrkcrtgcpmykvvgdcptwsdiecvh 180

OY 181 KESGTHSGEAPAVEETVTSPTSPASCSLSGIIIGTVAAVLLIVAVFCKSLMKV 240
 || |||||
 Db 181 ke-----sglllgvtvaavllivavfckslmkv 211
 OY 241 LPYLKIGCSGGGDERDRSSORPGAEADNVNLNEIVSLQPTQVPEQMEVQEPAPETGV 300
 |||||
 Db 212 lpylkigcsgggddpervdrssqrpqadnvlneivslqptqvpqemvqepapetgv 271
 OY 301 NMLSPSESEHLEPFAERSORRLVPAHNEGDPETLRQCFDPAIDVDPDSMEPLMRK 360
 |||||
 Db 272 nmlspseehllepfaersqrrllvpanegdpetlrqcfddadlvpdsweplmrk 331
 OY 361 LGIMDNEIKVAKAEAGHRDLYTMLIKWVKTGDRASVHTLDALETLGERLAKOKIED 420
 |||||
 Db 332 lgimdnelkvakaeaaaghrdltlytmlikwvntgrdasvhtldaletlgerlakokied 391
 OY 421 HLSSGKFWYLEGNDASMS 440
 |||||
 Db 392 hlssgkfwylegnadsams 411

RESULT 10

Y00932 ID Y00932 standard; Protein; 411 AA.

XX AC Y00932;

DT 02-JUN-1999 (first entry)

XX DE Human DR5 protein sequence.

KW Human; DR5; DR5s; TRAIL-R3; apoptosis related condition; cancer; therapy;

KM autoimmune disease; viral infection; degenerative disorder;

KW amyotrophic lateral sclerosis; retinitis pigmentosa; ischaemic injury;

KM cerebellar degeneration; myelodysplastic syndrome.

XX OS Homo sapiens.

XX PN W09909165-A1.

XX PD 25-FEB-1999.

XX PF 14-AUG-1998; 98WO-US16945.

XX PR 15-AUG-1997; 97US-0055906.

XX PA (IDUN-) IDUN PHARM INC.

XX PI Alnemut ES;

XX DR WPI; 1999-181035/15.

XX DR N-PSDB; X27279.

PT Newly isolated polynucleotide encoding a mammalian TRAIL receptor protein - useful in for screening for (ant)agonists that modulate the apoptotic activity mediated by DR5 or TRAIL-R3 proteins

PS Claim 16; Page 58-60; 71pp; English.

CC This sequence is the human TRAIL receptor DR5 of the invention. An
 CC antibody against the TRAIL receptors is useful for detecting mammalian
 CC DR5 or TRAIL-R3 proteins in a sample. Recombinant cells are useful in
 CC bioassays for screening for (ant)agonists of DR5 or TRAIL-R3 proteins.
 CC (Ant)agonists identified by the assay are useful for modulating the
 CC apoptotic activity mediated by DR5 or TRAIL-R3 proteins. Apoptosis
 CC related conditions which are treated in this way, include cancer
 CC (e.g. lymphomas and carcinomas), autoimmune diseases (e.g. systemic lupus
 CC erythematosus and immune-mediated glomerulonephritis), viral infections
 CC (e.g. herpes virus, poxvirus and adenovirus), degenerative disorders
 CC (e.g. Alzheimer's disease and Parkinson's disease), amyotrophic lateral
 CC sclerosis, retinitis pigmentosa, cerebellar degeneration, myelodysplastic
 CC syndromes (e.g. aplastic anaemia) and ischaemic injury (e.g. myocardial

CC Infarction and stroke). The polynucleotides can also be used to treat
 CC these diseases. Antisense oligonucleotides to the DNA sequences can be
 CC used to form a composition that is useful for inhibiting expression of a
 CC human DR5 or TRAIL-R3 protein.

XX Sequence 411 AA;

Query Match 91.9%; Score 2137.5; DB 20; Length 411;

Best Local Similarity 93.0%; Pred. No. 3,1e-170; Indels 29; Gaps 1;

Matches 409; Conservative 0; Mismatches 2; Indels 29; Gaps 1;

OY 1 MEORQANAPAAAGARKRHGPGREARGARPGRVKTVLVAAVLLVSAESALITQOD 60
 |||||
 Db 1 meqrqnaapaagaarkrhgpgreargarpgrlrvpklvlvvaavlllvsaesalltqgd 60
 OY 61 LAPQORAPQQRSSPSBGLCPPHHISBDGDCISCKYGGDYSTHWMDLLFCLRCTCD 120
 |||||
 Db 61 lapqoravpqqrsspsbglcpphhisedgdciscckygdysthwmldllfclrctcd 120
 OY 121 SGEVELSPCTTRNTVCCCEGTFRREDSPKCRKCRGCPGMVKYGDCTPMSDIEGVH 180
 |||||
 Db 121 sgevelspcttrntvcccegtfrredspemckrcrkcgprgmvkvgdctpswdlecvh 180
 OY 181 KESGTHSGEAPAVEETVTSPTSPASCSLSGIIIGTVAAVLLIVAVFCKSLMKV 240
 |||||
 Db 181 ke-----sglllgvtvaavllivavfckslmkv 211
 OY 241 LPYLKIGCSGGGDERDRSSORPGAEADNVNLNEIVSLQPTQVPEQMEVQEPAPETGV 300
 |||||
 Db 212 lpylkigcsgggddpervdrssqrpqadnvlneivslqptqvpqemvqepapetgv 271
 OY 301 NMLSPSESEHLEPFAERSORRLVPAHNEGDPETLRQCFDPAIDVDPDSMEPLMRK 360
 |||||
 Db 272 nmlspseehllepfaersqrrllvpanegdpetlrqcfddadlvpdsweplmrk 331
 OY 361 LGIMDNEIKVAKAEAGHRDLYTMLIKWVKTGDRASVHTLDALETLGERLAKOKIED 420
 |||||
 Db 332 lgimdnelkvakaeaaaghrdltlytmlikwvntgrdasvhtldaletlgerlakokied 391
 OY 421 HLSSGKFWYLEGNDASMS 440
 |||||
 Db 392 hlssgkfwylegnadsams 411

RESULT 11

W88410 ID W88410 standard; Protein; 411 AA.

XX AC W88410;

XX DT 26-APR-1999 (first entry)

XX DE Human Apo-2 ligand.

KW Apo-2 ligand; Apo-2DCR; human; tumour necrosis factor receptor;

KM neurodegeneration; autoimmune disease; inflammation; cancer;

KM apoptosis; therapy.

XX OS Homo sapiens.

XX FH Key Location/Qualifiers

XX FT Peptide 1..53

XX FT Protein /note="signal peptide" 54..411

XX FT Domain /note="mature protein" 54..182

XX FT Domain /note="extracellular domain" 183..208

XX FT Domain /note="transmembrane domain" 209..411

XX FT Region /note="intracellular domain" 96..137


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FT      Region                               /note="cysteine-rich region"
FT      Domain                               /note="cysteine-rich region"
FT      Misc-difference                     /note="death domain"
FT      FT                                  /label="Met, Leu
FT      FT                                  /note="encoded by WTC"
XX      MO9858062-A1.
XX      23-DEC-1998.
XX      12-JUN-1998; 98WO-US12456.
XX      18-JUN-1997; 97US-0878168.
XX      (GETH ) GENENTECH INC.
XX      Ashkenazi AJ, Baker KP, Chuntharapal A, Gurney A;
XX      Kim KJ, Wood WI;
XX      WPI: 1999-095340/08.
XX      N-PSDB; V84352.
XX      New Apo-2DCR polypeptide - used for modulation and diagnosis of
XX      apoptosis, e.g. in neurodegeneration
XX      Example 5; Page 61-62; 88pp; English.
XX      This polypeptide comprises human Apo-2 ligand. The amino acid
XX      sequence was deduced from a nucleotide sequence (see V84352)
XX      produced from overlapping cDNA clones obtained from human kidney
XX      and pancreatic cDNA libraries. The invention relates to Apo-2DCR
XX      (see W88408), a novel member of the tumour necrosis factor receptor
XX      family that binds to Apo-2 ligand and is involved in apoptosis.
XX      Apo-2DCR polypeptides are used to modulate apoptosis of mammalian
XX      cells (claimed) e.g. in the treatment of neurodegeneration,
XX      autoimmune diseases and inflammation. The Apo-2DCR polypeptides
XX      are optionally used in conjunction with Apo-2 ligand, the
XX      bioavailability of which is increased by antibody-mediated blockade
XX      of Apo-2DCR.
XX      Sequence 411 AA:
SQ
Query Match          91.8%; Score 2135.5; DB 20; Length 411;
Best Local Similarity 93.0%; Pred. No. 4,6e-170;
Matches 409; Conservative 0; Mismatches 2; Indels 29; Gaps 1;
OY      1 MEQRCGNAPAAAGARRHGGPREARGARPGPRVPTLVVVAVALLVSAESALITQOD 60
DB      1 meqrgnmapaasgarkrhpgpreargarpglvtvkvallvsaesalltqgd 60
OY      61 LAPOQRAAPQOKRSSPSEGLCPGPHHISEGRCISCKYGODYSTHMDLFLCTRCTCD 120
DB      61 lapqraapqokrsspseglcpgphhisegrcisckygodysthmdlflctrtcd 120
OY      121 SCGEVLSPECTTRNTVCCBEGTFREEDSPENCRCRTGCPRGKAVVGDCTPSDIECVH 180
DB      121 scgevlspcttrntvccbegtfreedspencrcrtgcprgkavvgdctpsdiecvh 180
OY      121 sgevelspcttrntvccbegtfreedspencrcrtgcprgkavvgdctpsdiecvh 180
DB      121 sgevelspcttrntvccbegtfreedspencrcrtgcprgkavvgdctpsdiecvh 180
OY      181 KESGTHSGSAPAVEETVSSPCTPASPCSLGIITGVMAAVLVAVFVCSLSLMKKV 240
DB      181 kesgthsgsapaveetvsspctpaspsclgiitgvmaavlvavfvcsllsmkkv 240
OY      181 ke-----sgllgvtaavallvavfvcsllsmkkv 211
OY      241 LPTLKICSGGGDPBRVDRSSQRPAGEDNVLMIEIVSIIQPTVPOQEMEQVPAEPTGY 300
DB      241 lptlkicsgggdprvdrssqrpagednvlmieivsiiloqtpvpoqemevpaepgy 300
OY      212 lpylkgicsgggdprvdrssqrpagednvlmieivsiiloqtpvpoqemevpaepgy 271
DB      212 lpylkgicsgggdprvdrssqrpagednvlmieivsiiloqtpvpoqemevpaepgy 271
OY      301 NMISPESEHLEPAEAKNSQRRRLVPAPEGPTETLRQCFDFADLVFPDSEPLMKR 360
DB      301 nmispesehlepaeaknsqrrrlvpapegptetlrqcfdfadlvfpdseplmk 360
OY      272 nmispesehlepaeaknsqrrrlvpapegptetlrqcfdfadlvfpdseplmk 331
DB      272 nmispesehlepaeaknsqrrrlvpapegptetlrqcfdfadlvfpdseplmk 331

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OY      361 LGMDNEIKVAKAAGHRDTLYTMLIKWVKGRDASVHTLDALETGERLAKOKIED 420
DB      332 lglmneikvakaaghrdtytmlikwvkgrrdasvhtldaletgerlakokied 391
OY      421 HLLSGKFMYLEGNADSAMS 440
DB      392 hllsgkfmylegnadsams 411
RESULT 12
W83321
W83321 standard; Protein: 411 AA.
W83321;
16-MAR-1999 (first entry)
Human Apo-2 protein.
Human Apo-2; receptor; apoptosis; neurodegenerative disease; cancer;
tumour necrosis factor; TNF; tumour necrosis factor receptor; TNFR;
TNF cytokine.
Homo sapiens.
Key location/Qualifiers
FT Misc-difference 410 /label="unknown
FT FT /note="encoded by WTC"
XX      MO9851793-A1.
XX      19-NOV-1998.
XX      14-MAY-1998; 98WO-US09704.
XX      09-FEB-1998; 98US-0020746.
XX      15-MAY-1997; 97US-0857216.
XX      (GETH ) GENENTECH INC.
XX      Adams CW, Ashkenazi AJ, Chuntharapal A, Kim KJ;
XX      WPI: 1999-045228/04.
XX      N-PSDB; V72526.
XX      Human Apo-2 polypeptide inducing apoptosis - useful to treat
XX      conditions linked with decreased apoptosis e.g. cancer, and produce
XX      antibodies to increase or decrease apoptosis
XX      Claim 1; Fig 1; 134pp; English.
XX      The present sequence represents human Apo-2. Apo-2 can be used
XX      therapeutically to induce apoptosis in mammalian cells, and so is useful
XX      to treat conditions associated with decreased apoptosis e.g. cancer.
XX      Apo-2 is believed to be a new tumour necrosis factor (TNF) receptor
XX      (TNFR). TNF cytokines can induce apoptosis, thought to be initiated by
XX      binding to TNFRs, and Apo-2 triggered caspase-dependent apoptosis. It
XX      can be used to identify agents activating Apo-2, useful to treat
XX      mammalian cancer cells, and to produce Apo-2 chimeras useful
XX      therapeutically (e.g. those containing immunoglobulin sequences can be
XX      inhibit apoptosis) or diagnostically (e.g. those comprising an epitope
XX      tag polypeptide allow Apo-2 detection and purification using anti-tag
XX      antibodies). It can be used to produce antibodies which can be combined
XX      with a (particularly pharmaceutically acceptable) carrier in compositions
XX      or used to produce dimeric molecules (especially homodimeric molecules
XX      comprising first and second Apo-2 antibodies). Agonistic (especially
XX      single-chain) antibodies can be administered to induce apoptosis in
XX      mammalian cancer cells, and antagonistic antibodies used to block
XX      excessive apoptosis (e.g. in neurodegenerative diseases). Apo-2
XX      antibodies may also be used diagnostically e.g. to detect Apo-2
XX      expression in cells/tissues and in Apo-2 purification.

```

XX Sequence 411 AA;

Query Match 91.8%; Score 2135.5; DB 20; Length 411;
Best Local Similarity 93.0%; Pred. No. 4.6e-170;
Matches 409; Conservative 0; Mismatches 2; Indels 29; Gaps 1;

QY 1 MEORGNMPPASGARRKRGPGREARGPGRVKTLLVVAALLVSAESALITOOD 60
DB 1 meqrqnapaasgarkrhpgpreargarpglrvpklvlvaavallivsaealltqgd 60
QY 61 LAPQGRAPQOKRSSPSGELCPRGHHISEDGRDCISCKYGGDYSTHMDLFLCRLCTCD 120
DB 61 lapqgrapqokrsspsgclcprrghisedgrdciscyggdysthmdllfclrlctcd 120
QY 121 SGEVELSPCTTTRNTVCCOEEGTFRFEDSPENCKRCRTGCPGMVKVGDCTPMSDIECVH 180
DB 121 sgevelspctttrntvccoeegtfreedspemcrkrcrtgpcgmkvvgdctpmsdiecvh 180
QY 181 KESGTRHSGEAPAVEETVTSFGTPASPCSLSGIIIGYVAAVLVAVFVCKSLMKKV 240
DB 181 ke-----sglllyvtvaavllvaavfvcslmkkv 240
QY 241 LPYLKIGISGGGDEPERVDRSSORPGAEADNVLEIVSLQPTQVEQEMVEQEPAPETGV 300
DB 241 lpylkigisgggdepervdrssorpgaednvlneivslqptqvqeemveqepaepetgv 300
QY 212 lpylkigisgggdepervdrssqrpgaednvlneivslqptqvpegemeveqepaepetgv 271
DB 301 NMLSGESEHLEPAEARSQRRLVLPANEGDPETELRQCDFDADLVFPDSWEPLMRK 360
DB 272 nmlsgesehlepaearsqrrllvpanegdpetelrqcdfdadvlpfswepmlmrk 331
QY 361 LGIMDNEIKVAKAEAGHRDLYTMLIKWVNKTGRDASVHTLLDALETGLERLAKOKIED 420
DB 332 lglm dneikvakaaghrdlytmlikwvntgrdasvhtlldaletglerlakokied 391
QY 421 HLLSSGKFMYLEGNADSAMS 440
DB 392 hllssgkfmylegnadsams 411

RESULT 13
ID Y55805 standard; Protein; 411 AA.
XX AC Y55805;
XX DT 29-FEB-2000 (first entry)
XX DE Human Apo-2 polypeptide.
XX KW Apo-2 polypeptide; immunization; antigen; polyclonal antibody; cancer; monoclonal antibody; Apo-2L receptor; therapy; apoptosis; autoimmune; immune-mediated cell death; neurodegenerative; inflammatory.
XX OS Homo sapiens.
XX FH Key location/Qualifiers
FT Misc-difference 410 /label= unknown
FT /note= "encoded by WTG"
XX PN WO9964461-A2.
XX PD 16-DEC-1999.
XX PF 10-JUN-1999; 99WO-US13197.
XX PR 12-JUN-1998; 98US-0096637.
XX PA (GETH) GENENTECH INC.
XX PI Ashkenazi AJ, Chuntharapai A, Kim KJ;

XX WPI: 2000-097520/08.
DR N-PSDB: 239630.

PT Preparation of antibodies using 2 or more different antigens, used for
PT producing antibodies against Apo-2 ligand receptors useful for inducing
PT apoptosis, particularly in cancer cells

PS Disclosure: Fig 5; 57pp: English.

CC The invention provides a method for producing antibodies (Abs) by
CC immunizing an animal with at least two different antigens. The method
CC comprises: (a) immunizing an animal with at least two different antigens,
CC to generate polyclonal Abs against each antigen in the animal; (b)
CC preparing monoclonal Abs (MAbs) using immune cells of the above animal;
CC and(c) screening the MAbs to identify one or more MAbs which bind to each
CC antigen. The Abs obtained are Apo-2L receptor (ant)agonists and can be
CC used for therapy. The Apo-2L receptor Abs can be used for enhancing
CC immune-mediated cell death in cells expressing Apo-2L receptors.
CC Agonistic Abs which specifically cross-react with 2 or more different
CC Apo-2L receptors can be used for inducing apoptosis in mammalian cancer
CC cells. Antagonistic Abs can be used for blocking apoptosis, e.g. in
CC neurodegenerative disease, or to block potential autoimmune/inflammatory
CC effects of Apo-2 resulting from NF-approx.KB activation. The Abs can also
CC be used for detection, diagnosis and affinity purification. The method
CC can reduce the number of animals that need to be immunized and sacrificed
CC in order to make 2 or more MAbs with differing antigen-binding
CC specificities. The present sequence represents a human Apo-2 polypeptide.

XX Sequence 411 AA;

Query Match 91.8%; Score 2135.5; DB 21; Length 411;
Best Local Similarity 93.0%; Pred. No. 4.6e-170;
Matches 409; Conservative 0; Mismatches 2; Indels 29; Gaps 1;

QY 1 MEORGNMPPASGARRKRGPGREARGPGRVKTLLVVAALLVSAESALITOOD 60
DB 1 meqrqnapaasgarkrhpgpreargarpglrvpklvlvaavallivsaealltqgd 60
QY 61 LAPQGRAPQOKRSSPSGELCPRGHHISEDGRDCISCKYGGDYSTHMDLFLCRLCTCD 120
DB 61 lapqgrapqokrsspsgclcprrghisedgrdciscyggdysthmdllfclrlctcd 120
QY 121 SGEVELSPCTTTRNTVCCOEEGTFRFEDSPENCKRCRTGCPGMVKVGDCTPMSDIECVH 180
DB 121 sgevelspctttrntvccoeegtfreedspemcrkrcrtgpcgmkvvgdctpmsdiecvh 180
QY 181 KESGTRHSGEAPAVEETVTSFGTPASPCSLSGIIIGYVAAVLVAVFVCKSLMKKV 240
DB 181 ke-----sglllyvtvaavllvaavfvcslmkkv 211
QY 241 LPYLKIGISGGGDEPERVDRSSORPGAEADNVLEIVSLQPTQVEQEMVEQEPAPETGV 300
DB 212 lpylkigisgggdepervdrssorpgaednvlneivslqptqvqeemveqepaepetgv 271
QY 301 NMLSGESEHLEPAEARSQRRLVLPANEGDPETELRQCDFDADLVFPDSWEPLMRK 360
DB 272 nmlsgesehlepaearsqrrllvpanegdpetelrqcdfdadvlpfswepmlmrk 331
QY 361 LGIMDNEIKVAKAEAGHRDLYTMLIKWVNKTGRDASVHTLLDALETGLERLAKOKIED 420
DB 332 lglm dneikvakaaghrdlytmlikwvntgrdasvhtlldaletglerlakokied 391
QY 421 HLLSSGKFMYLEGNADSAMS 440
DB 392 hllssgkfmylegnadsams 411

RESULT 14
ID Y00934 standard; Protein; 350 AA.
XX

AC Y00934;
 XX
 XX 02-JUN-1999 (first entry)
 XX
 DE Human DR5 protein sequence.
 XX
 KW Human; DR5; TRAIL-R3; apoptosis related condition; cancer; therapy;
 KW autoimmune disease; viral infection; degenerative disorder;
 KW amyotrophic lateral sclerosis; retinitis pigmentosa; ischemic injury;
 KW cerebellar degeneration; myelodysplastic syndrome; splice variant.
 XX
 OS Homo sapiens.
 XX
 PN WO9909165-A1.
 XX
 PD 25-FEB-1999.
 XX
 PF 14-AUG-1998; 98WO-US16945.
 XX
 PR 15-AUG-1997; 97US-0055906.
 XX
 PA (IDUN-) IDUN PHARM INC.
 XX
 PI A1nemr1 ES;
 XX
 DR WPI: 1999-181035/15.
 DR N-PSDB: X27281.
 XX
 PT Newly isolated polynucleotide encoding a mammalian TRAIL receptor
 PT protein - useful in for screening for (ant)agonists that modulate
 XX the apoptotic activity mediated by DR5 or TRAIL-R3 proteins
 XX
 PS Claim 16; Fig 5; 71pp; English.
 XX
 CC This sequence is the human TRAIL receptor DR5 of the invention. An
 CC antibody against the TRAIL receptors is useful for detecting mammalian
 CC DR5 or TRAIL-R3 proteins in a sample. Recombinant cells are useful in
 CC bioassays for screening for (ant)agonists of DR5 or TRAIL-R3 proteins.
 CC (Ant)agonists identified by the assay are useful for modulating the
 CC apoptotic activity mediated by DR5 or TRAIL-R3 proteins. Apoptosis
 CC related conditions which are treated in this way, include cancer
 CC (e.g. lymphomas and carcinomas), autoimmune diseases (e.g. systemic lupus
 CC erythematosus and immune-mediated glomerulonephritis), viral infections
 CC (e.g. herpes virus, poxvirus and adenovirus), degenerative disorders
 CC (e.g. Alzheimer's disease and Parkinson's disease), amyotrophic lateral
 CC sclerosis, retinitis pigmentosa, cerebellar degeneration, myelodysplastic
 CC syndromes (e.g. aplastic anaemia) and ischemic injury (e.g. myocardial
 CC infarction and stroke). The polynucleotides can also be used to treat
 CC these diseases. Antisense oligonucleotides to the DNA sequences can be
 CC used to form a composition that is useful for inhibiting expression of a
 CC human DR5 or TRAIL-R3 protein.
 XX
 SQ Sequence 350 AA:
 Query Match 76.7%; Score 1785; DB 20: Length 350;
 Best Local Similarity 79.1%; Pred No. 6.5e-141;
 Matches 348; Conservative 0; Mismatches 2; Indels 90; Gaps 1;
 OY 1 MEOGONAPASGARRKRRGPPREARGARPPRPXTLVVAAVLLVSAESALITQOD 60
 DB 1 megrgnapaasgartrkhrpgpreargarpgrlrvpklvlvvaavallvsaesalltqgd 60
 OY 61 LAPQQAQAQKRRSSSEGLCPGGHHISDGRDCISCKGQDYSTWMDLFLCRLTRCD 120
 DB 61 lapqgvaqgkrrsspsglcpghhisdgrdcisckygdydstwmdllfcltrcd 120
 OY 121 SGVEVLSPTCTTNTWCQCEEGFREDESPEMCRKRCGCPRGKVVGVGCTPMSDIECVH 180
 DB 121 sgvevlsptcttnvwcqceegfiredspemcrkrcgcpgrkvvgvcctpsdiecvh 180
 OY 181 KESGTHSGEAPAVEETVSSPCTPASPSLSGIIIGVVAAVLLVAVFVCKSLMKRV 240
 DB 181 kesgthsggapaveetvsspctpaspslsqiiigvtvaavlllavfvckslmwkv 240

DB 181 kesgthsggapaveetvsspctpaspslsqiiigvtvaavlllavfvckslmwkv 240
 OY 241 LPYLKIGICGGGDPPEVRSSORPGAEENVLEIYSIIOPVPOQEEVQEPAPPTGV 300
 DB 241 lpylkigicgggdppevrssorpgaednvleivsiilpvcvpeqevqepaptg- 299
 OY 301 NMLSPGESEHLEPAEERSQRRLVLPANEGDPTELRQCFDDFADLVLPFSMEPLMRK 360
 DB 300 -----
 OY 361 LGIMNEIVAKAEAGHRDTLYTMLIKWVNTGRASVHTLDALETIGERLAKQIED 420
 DB 300 -----vntgrdasvhtldaletlgerlakqied 330
 OY 421 HLSSGKFMYLEGNADSAMS 440
 DB 331 hlssgkfmylegnadsams 350
 RESULT 15
 ID W76828
 W76828 standard; Protein: 303 AA.
 XX
 AC W76828;
 XX
 DT 25-JAN-1999 (first entry)
 XX
 DE Human TR6 partial protein.
 XX
 KW TR6; tumour necrosis factor related receptor; human; treatment; stroke;
 KW inflammation; arthritis; septicemia; autoimmune disease; restenosis;
 KW transplant rejection; infection; ischemia; brain injury; bone disease;
 KW acute respiratory disease syndrome; acquired autoimmune disease syndrome;
 KW AIDS; cancer; atherosclerosis; Alzheimers disease.
 XX
 OS Homo sapiens.
 XX
 PN EP870827-A2.
 XX
 PD 14-OCT-1998.
 XX
 PF 23-DEC-1997; 97EP-0310562.
 XX
 PR 22-AUG-1997; 97US-0916625.
 PR 14-MAR-1997; 97US-0041230.
 PR 09-MAY-1997; 97US-0853684.
 XX
 PA (SMIK) SMITHKLINE BEECHAM CORP.
 XX
 PI Deen KC, Young PR;
 XX
 DR WPI: 1998-523156/45.
 DR N-PSDB: V63095.
 XX
 PT DNA encoding tumour necrosis factor receptor TR6 - and corresponding
 PT polypeptide, antibody, agonist, antagonist, etc
 XX
 PS Disclosure: Page 30-31; 34pp; English.
 XX
 CC This sequence represents a novel human tumour necrosis factor related
 CC receptor, TR6. TR6 polypeptides and polynucleotides can be used in the
 CC treatment of chronic and acute inflammation, arthritis, septicemia,
 CC autoimmune diseases (e.g. inflammatory bowel disease, psoriasis),
 CC transplant rejection, graft vs. host disease, infection, stroke,
 CC ischaemia, acute respiratory disease syndrome, restenosis, brain injury,
 CC (acquired autoimmune disease syndrome) AIDS, bone diseases, cancer (e.g.
 CC lympho-proliferative disorders), atherosclerosis and Alzheimers disease.
 XX
 SQ Sequence 303 AA:

